

A Lecture
ON
THE RELATION OF DIET TO HEALTH
AND DISEASE.

*SOME RECENT INVESTIGATIONS.**

BY

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THERE is but little doubt that some of the most important contributions to medicine in the last few years have come through the study of dietetics and nutrition. Advances in knowledge of these subjects have affected, or ought to have affected, the health of all mankind. I propose, therefore, as one whose lot it has been to be intimately connected with investigations on this subject, to relate something of the work that has been carried out in recent years. The limited time at my disposal only allows of a cursory glance at a few of the problems, but nevertheless I propose to draw attention not only to points which, from a practical aspect, may be regarded as settled, but also to results which suggest that there are other pathological conditions in which it is probable that dietetics will be found to play a dominant part.

What I want to do in this lecture is to give evidence which shows that diet, in addition to supplying material for growth and maintenance of the body and the necessary energy for the performance of its work, also contains two groups of substances—one which tends to produce pathological changes and ill health, and the other which helps the body to protect itself, not only against these toxic factors, but also against other disease-producing agents such as micro-organisms.

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I do not propose to discuss the energy-bearing constituents of diet—namely, proteins, fats, and carbohydrates. It is, of course, necessary that the amount of food eaten must contain a certain minimum of energy according to the work performed and heat lost by the individual. It is also true that these energy-bearing substances must include a minimum of biologically available protein both for growth and for maintenance. These are truisms which will always hold, whatever revolutionary discoveries may be made in the future in dietetics.

The history of the relation of food to disease was initiated by two discoveries. One was the work of Eijkman, who proved in 1897¹ that beri-beri was due to the absence from the diet of a substance found in many foods, but especially in the germ of cereals, and known later as the anti-beri-beri, or the antineuritic, vitamin, usually described at the present time as vitamin B₁. The other was the discovery of Holst and Frölich in 1907² that fresh foods, especially fruits and vegetables, contained a substance in whose absence from the diet the disease known as scurvy developed. This substance is now known as the anti-scorbutic vitamin, or vitamin C. Both these discoveries—the one which led to the establishment of the etiology of beri-beri, and the other to the etiology of scurvy—have been of great practical significance in themselves; but, for the moment, what I wish to emphasize is that they led to a new angle of thought—namely, that dietetic constituents, present maybe in infinitesimal amounts, are essential to the maintenance of health. Indeed, they led to investigations which ultimately made it clear that many of the commoner diseases of civilized man had a dietetic factor as a basis.

Neither beri-beri nor scurvy is a disease which is commonly found in Africa or Europe. Both are diseases associated with types of restricted diets uncommon in these continents—the one depending upon the consumption of an unbalanced diet of manufactured cereals treated in such a way as to lose the germ and the pericarp of the grain, and the other upon the absence of fresh food, especially of fresh fruit and vegetables. I have, it is true, seen a certain amount of scurvy since coming to Africa, especially in the natives associated with the gold-mining industry, but these cases were few in number, and I think that the medical officers in charge have the disease under control.

As regards beri-beri, I do not think there is much danger of this becoming a practical problem of any magnitude in Africa so long as the staple diet of the natives is whole unprepared maize, although, as I shall explain later, it seems to me likely that this form of dietary may lead to ill health because of certain toxic actions of cereals whose effects can be, and probably often are, prevented by other food constituents.

In order to supply evidence that foods commonly eaten by mankind include both protective and harmful elements,

I propose to refer to three practical problems: (1) the condition of the bones and teeth—the susceptibility of the former to rickets and the latter to caries; (2) degenerative changes in the central nervous system; (3) the liability of human beings to infection of the lungs, ears, nasal sinuses, genito-urinary tract, etc. Speaking as an investigator, it is probably superfluous for me to say that the results I shall describe, even when I relate them to disease in human beings, are the outcome of animal experiments. Only by means of such experiments is it possible to track down step by step and ultimately isolate the agent responsible for the phenomenon under investigation. When the results of animal experimentation become clear, it is then possible to test the beneficial effects as deduced on human beings.

DIETETIC FACTORS RESPONSIBLE FOR WELL CALCIFIED AND DEFECTIVELY CALCIFIED BONES AND TEETH.

Work of the last twelve years has cleared up to a surprising degree the factors responsible for well and badly calcified bones and teeth. It may be well to observe, however, that, although the practical problem is so far advanced that there is now no excuse for the appearance of rickets or dental hypoplasia in any normal child, there is practically no knowledge as to the intimate mode of action of the specific dietary constituents on the bones and teeth.

By far the most important factor producing well calcified bones and teeth is vitamin D. It seems not unreasonable to say that, no matter what the constituents of the diet—assuming, of course, that they are natural foods—a sufficiency of vitamin D will ensure perfect calcification of bones and teeth. Of course, since these tissues are largely made up of calcium phosphate, it is necessary that there should be some calcium and phosphorus in the food, but the amount can be surprisingly low and yet, with an abundance of vitamin D, they will be retained in the body and incorporated in the tissues. On the other hand, if the vitamin D intake is very deficient and the body is not exposed to sunlight, however much calcium and phosphorus there is in the diet, defectively calcified teeth and bones will result. There are occasions, however, when the influence of the calcium and phosphorus intake is of greater importance—for instance, when the vitamin D intake is moderate but insufficient in amount. The best example of this is seen when the main dietetic constituent carrying vitamin D is butter, a food containing an irregular but usually comparatively small amount of the vitamin. In this circumstance the addition of calcium salts, either as carbonate or phosphate, results in great improvement of bones and teeth. It would be expected from this statement that the calcifying properties of whole milk would be greater than those of the butter which can be prepared from it. This is certainly the case, partly because a little of the vitamin D is left behind in the separated milk and

also because most of the calcium of the milk remains after the separation of the butter.

The relation of vitamin D and calcium and phosphorus intake on calcification can be briefly summarized as follows: (1) When the vitamin D intake is high and the calcium and phosphorus intake low, perfect calcification of bones and teeth will ensue. (2) When the vitamin D intake is moderate, increasing the calcium and phosphorus intake will improve the calcification of bones and teeth. (3) When the vitamin D intake is very low, however high the calcium and phosphorus intake, imperfect calcification of bones and teeth will result, although not as imperfect as would have been the case had the calcium intake been low.

So far only those food factors aiding calcification have been mentioned. One group of foods, however, is outstanding because it interferes with the deposition of calcifying salts in bones and teeth. Those foods are the cereals. There is a wide difference between cereals in this respect. For instance, so far as animal experiments are concerned, oatmeal is the worst of all examined, and white flour interferes least with the calcifying process. Intermediate between these are maize, rye, barley, and rice. The embryo or germ of wheat and maize, and probably of other grains, has this baneful effect more developed than the endosperm. The germ of rye has vitamin D (in small quantities) as well as the substance interfering with calcification, and these actions can be separated owing to the solubility of vitamin D in alcohol. In spite of great endeavour, it has so far proved impossible to obtain information as to the chemical nature of the substance responsible for this effect of cereals. It is not associated with the carbohydrate nor with the fat. There is a possibility that it is in some way bound up with a protein, but this is by no means certain. As regards this anticalcifying effect of cereals there is one point I should wish to emphasize, because I believe it is of local interest in Kenya. Much has been said in recent years as to the significance of the mineral content of the diet, and various diseases of cattle have been ascribed to deficiencies of these, especially of calcium, phosphorus, and iodine. Now I have stated that of all cereals and cereal products tested, oatmeal and grain embryo interfere most strongly with the deposition of calcium and phosphorus in bones and teeth. It is at the same time well known that these grain products are far richer in calcium and phosphorus than such a substance, for instance, as white flour. Thus we have foods which, while they contain a more abundant supply of Ca and P, may in the absence of sufficient vitamin D result in a smaller retention of these elements in the growing bones and teeth. In other words, a greater deficiency of calcium and phosphorus in the body can be brought about by diets which actually contain more of these substances, so that an analysis of mineral intake may be quite misleading as to the efficacy of a diet in adequately supplying these substances to the tissues.

It may be well to emphasize, however, that the calcifying effect of vitamin D, whether it forms part of the diet or whether it is supplied to the body as the result of the activation by sunlight of ergosterol in the skin, will always, if present in sufficient quantity, antagonize the anti-calcifying effect of cereals. Thus, although the diet of the native is largely composed of maize, so long as his skin is unprotected from the sun's rays his bones and teeth will remain well calcified. If, in the course of his civilization, he adopts European habits of clothing, especially in childhood, then his bones and teeth may be as badly calcified as are those of the average European. On the other hand, when Europeans provide abundant vitamin D in the diets of their children, just so soon will their teeth and bones approximate in structure to those of the native as found at present.

Caries of the Teeth and Diet.

European teeth are generally badly calcified, and it would seem likely that this defective calcification is in some way related to caries. When teeth are well calcified, as in the average African native, they are white and shiny, and evenly arranged in powerful well-grown jaws. In the European only too often are the teeth discoloured, rough, and unevenly arranged. The following table gives an idea of the general relationship between the structure of teeth and susceptibility to caries in the case of English children.

The Relation of Structure to Caries in 1,036 Deciduous Teeth of English Children.

Teeth.	Defective in Structure.	Carious.
Incisors ...	14.4 per cent.	20.8 per cent.
Canines ...	54.5 ,,	46.2 ,,
First molars ...	73.1 ,,	81.9 ,,
Second molars ...	91.9 ,,	87.1 ,,

The teeth were first examined for caries, and were then ground down to thin slices and their minute structure determined by microscopic examination.

It will be seen from this table (1) that both caries and defective structure are very common, (2) that the least defective in structure (the incisors) are the least carious, while the most defective in structure (the molars) are the most carious.

As a matter of fact, these investigations made by May Mellanby showed that, although on the whole there was a close relationship between the structure of the teeth and caries, this was not absolute, for there were about 10 per cent. exceptions.³ Thus some teeth were imperfect in structure and yet free from caries, while others were good in structure and yet carious. The probable explanation of this was again brought to light by animal experiment. It is well known to all that teeth wear down as the result of attrition according to the degree of hardness of the food

eaten. In response to attrition the teeth normally react by producing a layer of secondary dentine adjacent to the dental pulp. By this means the pulp is protected from direct exposure to the food. It was found in dogs that the type and amount of secondary dentine produced as the result of artificial attrition depended on the type of food eaten at the time. Thus a diet of high calcifying qualities resulted in abundant well-formed secondary dentine, while a diet of poor calcifying qualities—that is, one with deficient vitamin D and much cereal—produced either no secondary dentine or a poorly calcified type of this tissue. Now human teeth when attacked by caries also respond by producing secondary dentine, which may be abundant and well formed or deficient and badly formed. When the exceptions in the children's teeth were examined from the point of view of secondary dentine it was usually found that badly formed teeth (primary dentine and enamel) when free from caries had well-formed secondary dentine, while well-formed teeth with caries usually had badly formed secondary dentine. Thus it would appear that, not only is the original formation of the teeth important as regards incidence of caries, but that, after full eruption and formation, teeth alter in their resistance to a bacterial onslaught according to the diet eaten. Thus a child may have a poor diet resulting in badly formed teeth, but at a later stage the calcifying qualities may improve and so increase the resistance of the teeth to caries. Similarly, well-formed teeth may lose their resistance when the diet becomes defective, and so become more susceptible to caries. The final proof that this actually occurred in children was also demonstrated by May Mellanby and C. L. Pattison, who showed that even badly formed teeth attacked by caries could increase their resistance to such an extent that the carious process was delayed or even arrested if these children were given diets very rich in vitamin D (irradiated ergosterol).⁴ This addition was made to the food of one batch of children, while another similar batch received the same food without the additional vitamin. The children receiving extra vitamin D not only showed great resistance to caries in the sound teeth as compared with the control children, but in many cases the active caries was actually arrested. (Sections of teeth showing arrest of caries produced by vitamin D were shown by lantern slides.)

To sum up: Well calcified teeth can be produced by the ingestion of sufficient vitamin D during the formation of the teeth. (2) Well calcified teeth are less susceptible and badly calcified teeth are more susceptible to caries. (3) Independently of their original structure, the inclusion of sufficient vitamin D raises the resistance of teeth to caries and may even arrest the carious processes, whereas diets deficient in this substance, especially if they contain much cereal, allow a lowered resistance to caries and a more rapid development of this condition.

FOOD AND THE CENTRAL NERVOUS SYSTEM.

It has long been known that diet has a special relation to the peripheral nerves, and, in particular, that the anti-neuritic vitamin or vitamin B₁ is implicated in this respect. I do not, however, wish to speak on this point, but to describe some results we have obtained in Sheffield which seem to show that diet has important effects on the central nervous system in quite another way. Some of these results are too recent to allow any definite deduction as to their practical or clinical significance, but they seem to me to be sufficiently suggestive to warrant description here.

In investigating the action of cereals on the formation of bones (experiments referred to above) we were impressed by the fact that some of the dogs developed severe incoordination of movement, often associated with and followed by weakness of the hind legs.¹⁴ When the nervous system of these animals was examined histologically by Marchi's method a scattered degeneration of the cord was often found, of such a nature that it suggested a subacute combined degeneration. On attempting to track down the conditions associated with this degenerative change in the nervous system we found (1) that it most often occurs in animals receiving much cereal, and especially in those whose diet includes the germ or embryo of grains; (2) that it is only found in animals receiving a diet deficient in fat-soluble vitamins.

In order to come more closely to grips with the problem, recourse was made to the use of ergot in the diet. The fact that ergot of rye produces degenerative changes in the cord has long been known, for these changes have been described in human beings affected by nervous ergotism—a condition which is very fatal and appears in epidemic form occasionally in European countries where rye is the main type of cereal eaten. Many attempts have been made by previous investigators to produce nervous ergotism in animals, but the success obtained has been very irregular in all types of animals, and nobody has understood why such disagreement in general results should have occurred. Incidentally, the curious distribution of nervous ergotism in epidemic form has never been understood. On the whole, it attacks the poorer people in times of famine, but it picks out, apparently without any discrimination, some members of a family and leaves others untouched. We soon suspected the apparent reason for this, for degenerative changes in the cord do not depend only on the presence of ergot in the diet, but also on the absence of a protective agent of the nature of a fat-soluble vitamin, probably vitamin A or a closely associated vitamin. The protective agent was not vitamin D, for ergot itself was found to contain vitamin D. If, however, cabbage, which contains little or no vitamin D, or mammalian liver oil (rich in A but poor in D) was added to the diet, then ergot left the cord untouched. Other substances containing vitamin A, such as egg yolk, butter, or cod-liver oil, also prevent nervous

ergotism in dogs. Vitamin D in the form of irradiated ergosterol will not in itself prevent the pathological condition. These results probably afford the explanation of the arbitrary way in which nervous ergotism develops in human beings. It develops in times of famine and distress because not only is the rye ergotized but poverty prevents the consumption of such protective substances as milk, eggs, and green vegetables. If, however, any individual has a good supply of vitamin A in the liver and other organs, the nervous changes will not be produced until these reserves are used up. It seems probable, therefore, that ergotism of the nervous system can be prevented in human beings by the inclusion in the diet of sufficient sources of vitamin A.

Having found that the degenerative changes in the cord in experimental ergotism were dependent on the absence of a protective dietetic factor, attention was again directed to the action of grain embryo and other cereals. It was found possible to produce the pathological condition by rye germ unaffected by the *Claviceps purpurea*. That is to say, that the nerve toxin in ergotized rye germ is present merely in exaggerated amounts as compared with normal rye germ. It has not proved possible, however, to obtain without fail the nerve degeneration by means of pure grain products in all dogs. Some litters have remained without obvious degenerative changes of the cord even when diet has included much wheat embryo and the vitamin A intake has been small. The negative results seem to depend on the litter of puppies and not on the specimens of wheat germ tested. What the explanation of this resistance in families is has not been ascertained. It may be that in some cases the maternal diet has been so good as to give the resistant litters a larger reserve of the protective substance (vitamin A) in their livers. Only further work will clear up this problem.

It may be said that, so far as the experiments can be interpreted, most cereals examined contain this toxic substance, even white flour, but there is much more in the embryo of the wheat, a fraction of the grain separated off in the manufacture of white flour. Oatmeal has also been found to contain this nerve "toxamin" (I have introduced the word "toxamin" to describe substances of unknown composition which have harmful effects in the body and which can be antagonized by specific vitamins. See also the anticalcifying toxamin referred to above, which can be antagonized by vitamin D.)

The question now arises, What is the clinical significance of these facts? So far as nervous ergotism in man is concerned the importance of the results described above is obvious. The three other conditions best recognized in which subacute combined degeneration of the cord arises are: (a) lathyrism, (b) pellagra, (c) pernicious anaemia.

(a) *Lathyrism*.—As regards lathyrism, I have had no

experimental or clinical experience of the condition. It is a nervous disease often found on a large scale in the North-Western Provinces of India, and is apparently due to a diet containing a large proportion of *lathyrus* peas. Experiments have been carried out on animals by many people, including Acton,⁵ Anderson, Howard, and Simonsen,⁶ and Stockman,⁷ but there is considerable discrepancy in the results obtained. It seems to me, on the analogy with the experiments quoted above on ergotism, that this discrepancy is probably due, in part at least, to the same cause as that responsible for the irregularity of the earlier animal experiments on nervous ergotism—namely, that the nerve degenerative changes are dependent on a toxic substance in the *lathyrus* peas, but that the condition is prevented if there is a sufficiency of a “protective” substance in the other part of the diet. It may be the same protective substance as in nervous ergotism—namely, vitamin A—but this is only surmise at the present time. The whole picture of lathyrism, so far as I understand it, suggests, indeed, that the toxic agent of the *lathyrus* pea is of a similar nature to that of ergot nerve toxin; but this again is supposition. It is true that Stockman produced lathyrism in a monkey when the diet included “one ounce of fresh cabbage or a little fruit” daily, but fruit would be of no value as a protective agent on the hypothesis suggested, and the amount of cabbage was not only small but there is no statement as to how often this was given in the food and how often the fruit. The disease of lathyrism needs further investigation from this new angle.

(b) *Pellagra*.—It has been assumed that the later investigations of Goldberger⁸ on pellagra have cleared up completely the etiology of this disease. There is, indeed, no question but that, so far as the skin lesions are concerned, Goldberger's work has definitely shown the importance of the pellagra-preventing factor now usually known as vitamin B₂. It is impossible, however, to consider the nerve degenerations in the cord of pellagrins together with the results above discussed on the effect of cereal and cereal products on the nervous system without wondering whether in pellagra also the degeneration of the cord is not associated with a “toxamin.” The almost constant association of a maize diet with pellagra increases this probability. Is vitamin B₂, or the pellagra-preventing factor, the same substance as the protective substance against nervous ergotism and the cord degeneration produced by cereals in the experiments described above? Sources of the pellagra-preventing factor in Goldberger's investigations included milk, meat, and yeast. So far as milk and meat fat are concerned these are also sources of vitamin A, which I have shown is a protective substance against nervous ergotism. The one real discrepancy between Goldberger's results on pellagra and mine on nervous ergotism is that according to him yeast cures

pellagra whereas it does not, in my work, prevent nervous ergotism. Yeast does not contain any vitamin A. There has been no suggestion up to the present that there is a positive pellagra-producing factor in maize responsible for the cord degeneration, but the results under discussion suggest that pellagra is possibly due to a positive harmful factor in certain cereals, including maize, and that this factor is in normal people prevented from having its baneful influence by a protective agent of the nature of a vitamin or possibly vitamins, including B₂ and A. I have been unable to obtain degenerative changes in the cord by yellow maize. This may be due to the fact that it contains vitamin A, or rather carotene, which acts in the same way as vitamin A.

(c) *Cord Degeneration in Pernicious Anaemia.*—The close relationship of the cord degeneration found in pernicious anaemia and the changes produced by cereals in dogs in the absence of vitamin A suggests a similarity in etiology. There is a further coincidence which is in line with this point of view. Pernicious anaemia is brought under control by liver and water-soluble extracts of liver. The nerve degeneration of ergotism and that produced by wheat germ or embryo can be prevented or, if developed, the condition greatly improved by the fat-soluble portion of liver. In my experience the blood changes in pernicious anaemia cannot be cured by the fat-soluble portion of liver. On the other hand, it has been recently claimed by Ungley and Suzman¹⁵ that the nerve symptoms of pernicious anaemia can be greatly improved by feeding whole liver. If so, it seems probable that it is the fat-soluble portion which exerts this effect on the cord. It is possible that both the blood changes and the cord degeneration in pernicious anaemia are due to failure on the part of the liver, the blood condition being due to the exhaustion of some specific water-soluble substance and the cord changes to a deficiency of a specific fat-soluble substance, maybe vitamin A as discussed above. Only further work will show whether pernicious anaemia has a positive dietetic causation similar to that found in cereals which produces nerve degeneration. It is interesting, however, to speculate, on the basis of the results described above, as to what extent these experimental methods of producing and preventing pathological changes in the cord by dietetic means will prove to be of practical value in aiding the solution of problems of disease commonly found in man.

THE PREVENTION AND CURE OF SOME INFECTIVE CONDITIONS.

I wish now to pass on to another aspect of this subject of diet and disease. So far I have dealt with the production of pathological changes in various organs by substances actually present in food and the prevention of these changes by other "protective" food elements. I shall now deal with pathological conditions produced by the invasion

of the body by certain micro-organisms and a method of preventing this invasion by specific dietetic means. This subject, again, is too new to allow any great claims to be made as to the extent of its possible application, but the results obtained seem to me to be sufficiently definite to warrant the belief that ultimately it will prove to be of great importance as a means of raising the resistance of the body to pathogenic micro-organisms and of gaining an insight into the subject of immunity.

Everybody who has been interested in the experimental side of dietetics and nutrition must have been struck by the susceptibility of animals to infection when eating defective diets. I called attention to this fact so long ago as 1919.⁹ At a later stage I became more interested in the subject as the result of an experience in the laboratory in which a large number of experimental dogs died of broncho-pneumonia.¹⁰ At the time my interest was particularly centred round bone calcification, but the incidence of the disease showed that the lung infection and the condition of the bones were independent, although both were related to fat-soluble factors. In other words, the susceptibility to lung infections did not depend on the absence of vitamin D, but probably on the absence of vitamin A. These results were published in 1926.¹⁰

More recently we have shown that young rats fed on a diet which, so far as is known, is complete except for vitamin A, die in the course of six to fifteen weeks, and on post-mortem examination are found to have developed one or more abscesses in different parts of the body. The relation of vitamin A deficiency to xerophthalmia has been known for many years, but our animals developed many other septic conditions, sometimes without any xerophthalmia. The more common seats of infection included the base of the tongue, the nasal sinuses, the middle ear, the lungs, the kidneys and bladder, the alimentary tract, and many other places. It was shown so long ago as 1922¹¹ by Mori that a peculiar effect of vitamin A deficiency is to produce various forms of hyperplasia of epithelium, and it is at these seats of hyperplastic change that the infective condition develops. More detailed facts of the relation of vitamin A to infection in rats and the history of the subject can be read in a paper published by H. N. Green and myself in the *British Medical Journal* in 1928.¹² It may be said that if sufficient vitamin A is given to these animals after having developed the infective condition recovery is often brought about. On the other hand, the inclusion of this vitamin in the diet prevents the development of the pathological state.

We were so impressed by the results of the animal experiments that Green and I determined to see whether vitamin A played any part in the resistance of the human body to infection. It seemed at first sight that this would probably be the case, because not only are the lesions

produced in rats very common in people in England—for example, septic nasal sinuses, middle-ear disease, genito-urinary infections, and pneumonic conditions—but the diet in this country is largely cereal and notoriously deficient in vitamin A. The difficulty was to find a disease due to bacterial invasion the investigation of which would yield results, definitely positive or negative, in a reasonable time. Most common infective conditions recover in any case, and in pneumonia the results are variable whatever the treatment. We decided to study the action of vitamin A in puerperal septicaemia, a disease in which the mortality rate is normally so high that a rapid decision could be made as to the efficacy of the treatment. As a control series of cases we took those patients who had entered the institution where the investigation was carried out, in the two years prior to the new treatment. In these two years 22 patients had been admitted from whose blood a growth of haemolytic streptococci had been obtained. Of these 22 patients 20 died, giving a mortality rate of 91 per cent. From the beginning we have treated with vitamin A 9 similar cases, and of these 8 have made complete recoveries. There have also been two other septicaemic patients, one with an infection of *Bacillus coli*, who recovered, and the other with a staphylococcal infection, who died. Thus, of the total 11 cases, 2 have died, giving a mortality rate of 18 per cent., as compared with the mortality rate of 91 per cent. in the control group. The results can be readily seen in the following table.

Type of Blood Infection.	Control Group of Cases.			Vitamin A Treated Cases.		
	No.	Deaths.	Mortality Rate.	No.	Deaths.	Mortality Rate.
Haemolytic Streptococci	22	20		9	1	
<i>Bacillus coli</i> ...	0	0		1	0	
Staphylococcus ..	0	0		1	1	
Total	22	20	92%	11	2	18%

It is true that the number of cases treated with large doses of vitamin A is not sufficiently great to allow the definite claim that this substance is a specific remedy for puerperal septicaemia. Nor were the cases of the intense fulminating type sometimes met with in this condition. On the other hand, we think there is strong evidence, especially taken in conjunction with the animal results, that vitamin A has a definite effect in raising the resistance of the body, both human and animal, to bacterial agencies, and that, in its absence from or deficiency in the body, the resistance to infection of this

type is greatly diminished. It is obviously necessary that this work¹³ should be repeated on a larger scale and extended to the treatment of other infective conditions, for its practical importance, if established, cannot be exaggerated.

What value these results, if established, may have to medical men in Africa is for you to determine. They may point to a method of reducing the high mortality rate in pneumonia among the natives as well as among Europeans. If it does act curatively in this condition, the probability is greater that the inclusion in the normal diet of sufficient quantities of vitamin A will prevent the disease as well as other infections of a similar bacterial nature. Rich sources of vitamin A are egg yolk, mammalian liver, cod-liver oil, and there is some in carrots, green vegetables, milk, butter, and suet. It may be well to add that vitamin A is a very unstable substance and is apt to disappear rapidly, especially in high concentrations.

I have endeavoured to supply you with evidence, both experimental and clinical, which shows how important is this subject of the relation of diet to disease. In particular, I have tried to demonstrate that food includes both harmful and protective constituents. In so far as the harmful substances mentioned are in the food itself, it appears that they can be neutralized in their action by the protective agencies. The protective agencies are of the nature of vitamins, and the two I have specially dealt with are vitamins A and D. The harmful factors are mostly associated with cereals and cereal products so far as present knowledge goes.

I wish especially to emphasize that this subject is only in its infancy, and that many of the facts I have dealt with here have still to be investigated more closely, partly because it is impossible as yet to decide what is their true clinical significance, and partly because there is no knowledge of the methods by which these substances exert their effect. So far as you in Kenya are concerned, it seems to me that these dietetic problems, especially those concerning the toxic action of cereals, may have special significance, for I cannot believe that your native population with its high cereal diet completely escapes those effects. It is true that the sunshine to which the African native exposes himself must tend to neutralize the anticalcifying effect of maize by supplying vitamin D, but I should expect the native who wears European clothing, especially in childhood, and remains on his maize diet to suffer accordingly. Similarly it seems to me probable that a deficiency of vitamin A might be present in many native diets, especially in the towns, and that pathological results would follow. I shall be interested to hear of any investigations which may be made in the future to see whether these hypotheses have a bearing on any of the problems of disease in Africa.

REFERENCES.

- ¹ Eijkman : *Arch. f. path. Anat.* (etc.), 1897, 149, 197.
- ² Holst and Frölich : *Journ. of Hyg.*, 1907, 7, 634.
- ³ Mellanby, M. : *Brit. Dental Journ.*, 1927, 48, 1481.
- ⁴ Mellanby, M., and Pattison, C. L. : *British Medical Journal*, 1928, ii, 1079.
- ⁵ Acton : *Indian Med. Gaz.*, 1922, 57, 241, 331, and 412.
- ⁶ Anderson, Howard, and Simonsen : *Indian Journ. of Med. Research*, 1924-25, 12, 613.
- ⁷ Stockman : (a) *Edinburgh Med. Journ.*, 1917, 19, 277 and 297; (b) *Journ. of Pharm. and Exper. Ther.*, 1929, 37, 43.
- ⁸ Goldberger, Wheeler, Lillie, and Rogers; *Pub. Health Rep.*, Wash., D.C., 1926, 41, 297.
- ⁹ Mellanby, E. : *Lancet*, 1919, i, 407.
- ¹⁰ Idem : *British Medical Journal*, 1926, i, 515.
- ¹¹ Mori : *Bull. Johns Hopkins Hosp.*, 1922, 33, 357.
- ¹² Green, H. N., and Mellanby, E. : *British Medical Journal*, 1928, ii, 691.
- ¹³ Idem : *Ibid.*, 1929, i, 984.
- ¹⁴ Mellanby, E. : *Journ. of Physiol.*, Proceedings, 1926, vol. lxi.
- ¹⁵ Ungley, C. C., and Suzman, M. M. : *Brain*, 1929, 52, 271.